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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/403,107	10/14/1999	PETER KUFER	3816-4000	6846

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	28

DATE MAILED: 03/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/403,107	KUFER ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-22,28,29,31,32 and 34-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-22,28,29,31,32 and 34-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Upon amendment to claims 31 and canceling claims 68-75 the restriction requirement mailed 8/27/02 is moot and vacated.

2. Claims 18, 20, 21, 28, 31, 32, 65, 67 have been amended and claims 68-75 have been canceled.

3. Claims 18-22, 28-29, 31-32, 34-67 are pending and under examination.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 18-22, 28-29, 31-32, 34-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 18 and those that depend from claim 18 are indefinite for reciting "essentially unprimed mature human B-lymphocytes" in claim 18 because the exact meaning of the phrase is unclear. Are the lymphocytes unprimed or not?

b. Claim 28 and those that depend from claim 28 are indefinite for reciting "functionally rearranged" in claim 28 because it is unclear what the VH and VLs are compared to. How are they rearranged if one does not know what they are compared to?

c. Claim 34, 36 and those claims that depend from claims 34 and 36 are indefinite for reciting "or at least one CDR" in claims 34 and 36 because it is not clear if the CDr is from the VH (in claim 34) or the VL (in claim 36) or from any VH or VL.

d. Claim 66 is indefinite for reciting "derived" because the exact meaning of the term is not clear. The term "derived" is not one which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The primary deficiency in the use of this phrase is the absence of a ascertainable meaning for said phrase. Since it is unclear how the constant region chains are to be derivatized to yield the class of derivatives referred to in the claims, there is no way for a person of skill in the art to ascribe a discrete and identifiable class of compounds to said phrase. In addition, since the term "derived" does not appear to be clearly defined in the specification, and the term can encompass proteins with amino acid substitutions, insertions, or deletions, chemically derivatized molecules, or even mimetics. In absence of a single defined art recognized meaning for the phrase and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

e. Claims 22 and 32 and those claims that depend on claims 22 and 32 are indefinite because in claim 22 it is not clear how the amino acid sequence can correspond to a nucleotide sequence and in claim 32 how the VH can comprise a sequence that is a DNA sequence or a VL that comprises a DNA sequence.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18-22, 28-29, 31-32, 34-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a human antibody comprising a human VH and a human VL domain wherein the antibody or binding fragment thereof comprises 6 DRS, three from the VH domain and three from the VL domain wherein the antibody or binding fragment binds a tumor antigen and compositions comprising such, does not reasonably provide enablement for a anti-human antigen receptor as broadly encompassed by the claims or a human antibody or fragment thereof that does not bind antigen or antibodies and fragments that do not contain a full set of 6 CDRs from the VH and the VL domain or pharmaceutical compositions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to any anti-human antigen receptor or a human antibody or fragment thereof that does not bind antigen (claims 18-19, 22, for example) or antibodies and fragments that do not contain a full set of 6 CDRs from the VH and the VL domain (claims reciting "at least one CDR") or pharmaceutical compositions.

The specification discloses only antibodies and antigen binding fragments that contain both a VH and a VL chain and the antibodies or fragments thereof bind antigen (see examples). The specification does not enable any antigen receptor as broadly claimed or antibodies which do not contain 6CDRs and bind antigen or pharmaceutical compositions.

The claims encompass any anti-human antigen receptor but the specification only discloses an antibody. The specification does not enable any other receptor.

Claim 28 encompasses VH and VL chains that have been functionally rearranged but the specification does not teach a functionally rearranged VH or VL wherein the antibody binds 17-1A.

The claims encompass antibodies which do not contain a full set of 6 CDRs or antibodies which do not bind antigen. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all

of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that proteins as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions have the required binding function. The specification provides no direction or guidance regarding how to antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Further, a fragment of an antibody can be a constant region, or just a light or heavy chain, which the heavy chain can be any one of the constant regions (CH1-3) and also may be the hinge region. However, the language also reads on small amino acid sequences which are incomplete regions of the antibody which does not have a binding function.

The claims as written as drawn to pharmaceutical compositions which read on in vivo treatment for cancer. However, the data presented to support the enablement of the claims is based on cell culture, in vitro studies.

One cannot extrapolate the teaching of the specification to the claimed invention because there is no guidance on or exemplification of any correlation between in vitro data and *in vivo*. The *in vitro* experimental data presented is clearly not drawn to subjects with tumor cells (see page 39). Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation in vivo. Without this control, cellular metabolism may be more constant in vitro but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary - type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal

or malignant cells in vivo are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Thus, based on the cell culture data presented in the specification, it could not be predicted that, in the *in vivo* environment, the antibodies would be used for treatment of cancer.

Further, One cannot extrapolate the teaching of the specification to the claims because it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para).

Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3).. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The formulation may be inactivated *in vivo*

before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the formulation. In addition, the formulation may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the formulation has no effect, circulation into the target area may be insufficient to carry the formulation and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the antibodies with a reasonable expectation of success.

Further claims reciting a pharmaceutical composition of an antibody that does not clearly state which antigen it binds is not enabled also because it would require undue experimentation to determine the affect of an antibody without knowing its target.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

8. Claim18-22, 28-29, 31-32, 34-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims recite an anti-human antigen receptor or functionally rearranged VH or VL (claim 28). The specification only discloses an antibody as an anti-human antigen receptor. The specification does not disclose any other anti-human antigen receptor wherein the phrase encompasses receptors for a multitude of antigens. The specification does not describe any receptors for antigens as broadly encompassed in the phrase. The specification additionally does not describe any "functionally rearranged" VH or VL or what VH or VL the genes were "functionally rearranged" from. Therefore, the specification does not describe elements encompassed by the claims.

9. Claim 28 and those depending on claim 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 28 was amended in the amendment filed 1/31/02 to recite "a human VH chain and a human VL chain that have been functionally rearranged". The amendment did not state where support for the amendment can be found. The claim was amended to remove "is derived from human sequences". The addition of the new limitation of "functionally rearranged" is not the same as "derived from" which encompasses obtained by or any alteration. The term "functionally rearranged" is not defined and as such does not mean the same as "derived". Applicant is required to provide specific support in the application as originally filed or remove the limitation from the claim.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 18-20, 28-29, 34-40, 43-45, 48-50, 53-54, 65, 67 are rejected under 35 U.S.C. 102(e) as being anticipated by Griffiths et al (U.S. Patent 5,885,793, 102e date 10/94).

The claims recite a anti-human antigen receptor being low immunogenic in humans comprising a VH and VL wherein the VH is derived from essentially unprimed mature human B lymphocytes and the VL are derived from naturally occurring B cells and the receptor binds a tumor antigen the receptor comprises a human VH and VL that have been functionally rearranged and comprises at least one CDR and compositions

comprising such and the receptor has a non-immunoglobulin fused to it and a biologically active molecule fused to it. The intended use as a pharmaceutical composition is given no patentable weight for this rejection.

Griffiths et al teach antibodies against self antigens such as CEA (se figure 2b and entire specification and Example 3) and the V genes are rearranged in vitro or in vivo (see column 2, lines 4-5, column 6, lines 15-20) and the antibody or ScFv can be fused to gene 3 or an enzyme or a constant region or another protein (see column 2, lines 29-30, column 4, lines 41-45, column 6, lines 45-51, column 15, line 45) and the source of the antibodies can be from unimmunized humans (see column 8, lines 63-65, column 9, lines 15-31).

The product is claimed in a product by process format wherein the VH and VL chains are derived from a certain source. The VH and VL chains are no different depending on the source of the chains. The B cells would have the VH and the VL chains and as such would not differ whether they were unprimed or not. Therefore the method in which the antibodies were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

12. Claims 18-20, 34-40, 43-45, 48-50, 65, 67 are rejected under 35 U.S.C. 102(e) as being anticipated by Kucherlapati et al (U.S. Patent 6,150,584, filed 10/96).

The claims have been described supra. The intended use as a pharmaceutical composition is given no patentable weight for this rejection.

Kucherlapati et al teach antibodies and antigen binding fragments wherein the antibodies are produced in zenomice and the antibodies bind tumor antigen (see column 10) and the antibodies can have a radioisotope conjugated to them (see column 7, line 3) and compositions comprising such.

The product is claimed in a product by process format wherein the VH and VL chains are derived from a certain source. The VH and VL chains are no different depending on the source of the chains. The B cells would have the VH and the VL chains and as such would not differ whether they were unprimed or not. Therefore the method in which the antibodies were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

13. Claims 18-21, 34-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoess et al (Proceedings of the American Association for Cancer Research 38page 30 abstract 198, 1997, Ids #3).

Claims 18-20, 34-37 have been described supra and claim 21 recites wherein the receptor recognizes the native 17-1A antigen.

Hoess et al teach antibodies which bind to the 17-1A antigen.

The product is claimed in a product by process format wherein the VH and VL chains are derived from a certain source. The VH and VL chains are no different depending on the source of the chains. The B cells would have the VH and the VL chains and as such would not differ whether they were unprimed or not. Therefore the method in which the antibodies were produced is immaterial to their patentability. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 18-21, 28-31, 34-41, 43-46, 48-51, 53-55, 57-59, 61-63, 65, 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al (U.S. Patent 5,885,793) as applied to claims 18-20, 28-29, 34-40, 43-45, 48-50, 53-54, 65, 67 above, and further in view of Gottlinger et al (Int, J. Cancer 38:47-53, 1986, IDS #3).

Claims 18-20, 28-29, 34-40, 43-45, 48-50, 53-54, 65, 67 have been described supra, the additional claims recite wherein the antigen is 17-1A and compositions comprising such.

Griffiths et al has been described supra. Griffiths et al does not teach the antigen 17-1A. This deficiency is made up for in the teachings of Gottlinger et al.

Gottlinger et al teach the tumor antigen 17-1a and antibodies directed to the antigen.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced antibodies against the 17-1a antigen of Gottlinger et al by the method of Griffiths et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced antibodies against the 17-1A antigen of Gottlinger et al by the method of Griffiths et al because Griffiths et al teach the antibodies can be directed to tumor antigens and it would have been obvious to produce antibodies to the 17-1A antigen since Gottlinger teach that the 17-1A antigen is a tumor antigen and is expressed in human carcinomas (see page 47).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

16. Claims 18-21, 34-41, 43-46, 48-51, 65, 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kucherlapati et al (U.S. Patent 6,150,584, filed 10/96) as applied to claims 18-20, 34-40, 43-45, 48-50, 65, 67 above, and further in view of Gottlinger et al (Int, J. Cancer 38:47-53, 1986, IDS #3).

The claims have been described supra.

Kucherlapati et al has been described supra. Kucherlapati et al does not teach the antigen 17-1A. This deficiency is made up for in the teachings of Gottlinger et al.

Gottlinger et al teach the tumor antigen 17-1a and antibodies directed to the antigen.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced antibodies against the 17-1a antigen of Gottlinger et al by the method of Kucherlapati et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced antibodies against the 17-1A antigen of Gottlinger et al by the method of Kucherlapati et al because Kucherlapati et al teach the antibodies can be directed to tumor antigens and it would have been obvious to produce antibodies to the 17-1A antigen since Gottlinger teach that the 17-1A antigen is a tumor antigen and is expressed in human carcinomas (see page 47).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703)

306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879